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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,631	02/19/2002	Paul Habermann	DEAV2001/0007USNP	2601

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
02/19/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/076,631	HABERMANN, PAUL	
	Examiner	Art Unit	
	ROBERT B. MONDESI	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Amendment filed December 12, 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-12 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-12 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the amendment filed December 12, 2007.

Status of the Claims

Claims 2-5 and13-26 have been canceled. **Claims 27-29** have been added. **Claims 1, 6-12 and 27-29** are currently pending and under examination.

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn due to applicants' response and amendment to the claims in amendment filed December 12, 2007.

Maintenance of rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6-12 remain rejected and **claims 27-29** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 27-29 are depended claims that have been added in or to address the rejection of the claims under 35 U.S.C. 101 and do not address issues with regards to

the rejection of the claims under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 1 and 6-12 remain rejected and **claims 27-29** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence prepared as described in Examples 1-3 of the specification and having the signal sequences as set forth at pages 17-18 of the specification, does not reasonably provide enablement for all the possible nucleic acid molecules suggested by the general formula of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

Claims 27-29 are depended claims that have been added in or to address the rejection of the claims under 35 U.S.C. 101 and do not address issues with regards to the rejection of the claims under 35 U.S.C. 112, first paragraph, as failing to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

Claim 1 remains provisionally rejected under the judicial created doctrine of obviousness-type double patenting as being unpatentable over claim 4 of US non-provisional application 10/076,634 (1634 Application).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8 and 11-12 remain rejected as written, because they do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, he naturally occurring products are considered nonstatutory subject matter.

The above rejections were explained in the previous Office actions.

Response to applicants' arguments

In regards to the rejection of claims under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, applicants assert that claim 1 is amended to simplify the molecule and exclude non-specific codons of Bn and generic or unspecified proteins previously recited as protein(Ym). Applicant respectfully submits that the simplified molecule can be said to even more adequately meet the written description requirement. Claims 6-12 ultimately depend from claim 1 and thus claimed inventions that further limit the invention claimed in claim 1. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Applicants' arguments have not been found persuasive. Presently the claims are drawn to a genus of nucleic acid molecules with substantial variation and when there is substantial variation within the genus and without any functional characteristics. The claims merely recite a structural formula for a product with any particular function and as such lack written description. It is recommended that applicants include language in claims pertaining to the functional characteristic of the genus. Note to applicants, transport peptide is merely a designation for a component of the final product and is not

an attempt on the part of applicants to specify the overall functional characteristics of the nucleic acid construct.

In regards to the rejection of the claims under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence prepared as described in Examples 1-3 of the specification and having the signal sequences as set forth at pages 17-18 of the specification, does not reasonably provide enablement for all the possible nucleic acid molecules suggested by the general formula of claim 1, applicants assert that claim 1 is amended to simplify the molecule and exclude non-specific codons of Bn and generic or unspecified proteins previously recited as protein(Ym). Applicant respectfully submits that the simplified molecule can be said to even more adequately meet the written description requirement. Claims 6-12 ultimately depend from claim 1 and thus claimed inventions that further limit the invention claimed in claim 1. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Applicants' arguments have been considered but have not been found persuasive. Still, as presently amended the claimed structural formula for the nucleic acid construct of the invention is drawn to an extremely large genus with practically no functional characteristics/limitations. Presently the claimed construct is not required to retain any function. As stated above, applicants' recitation of "transport peptide" is merely to indicate a variable component wherein many different peptides may be used. Presently a person skill in the art would not know how to use the invention commensurate with the scope of the claims. A person skill in the art would most

probably be able to make the claimed genus but would not be able to determine whether each particular species will retain the specific intended function (this being specially worrisome since there are no functional limitations in the claim).

Therefore the examiner still believes that it is considered to be an undue burden for a person skill in the art to test all the possible constructs that are represented by the claimed structural formula. A person skill in the art is well aware of the fact that even the slightest change in the sequence of a DNA molecule can lead to a complete loss of function. There is no information in the claims or in the specification that would explain to a person skill in the art as to which portion of the construct is essential for the intended function characteristics- and in a nutshell this is the Patent Offices' understanding of the "structure-function relationship".

To wit, it has long been known how to mutate proteins, but it has been similarly long been known that such mutations are not reasonably predictive of activity for any particular protein. For example, Rudinger (1976) Peptide Hormones, University Park Press, Baltimore, MD., pp. 1-7 discusses the peptide hormones and the characteristics of amino acids as components of the peptide hormones (TITLE). (It is noted that Rudinger discusses peptide hormones, but the general areas of unpredictability are common to all proteins.) In doing so, Rudinger notes that many amino acids may be grouped according to general characteristic (pp. 1-3), and many of these are also classified in two or more classifications (p. 3). Hence, simple mutations of "type" are not reasonably predictable, because there are multiple types to any particular amino acid. Moreover, Rudinger finds that the context of any amino acid is important for structure

(pp. 3-4), and that therefore, simple deletions, insertions, or substitutions are also not reasonably predictable, because not only is "type" important, but context is also important, having longer-range effects than that of simply type. Further, Rudinger discusses the mechanisms of information transfer (e.g, binding and effecting a receptor, which is analogous to any protein binding anything and causing any particular effect) (pp. 4-5). In doing so, Rudinger finds that there exist "patterns" on molecules for recognition, which may involve amino acids close by in the amino-acid polypeptide sequence, or far away (Id.). As such the conformation of the whole molecule is important, and any particular amino acid change, deletion, or addition, may alter the conformation of the molecule enough to affect any particular binding and effect on another molecule.

In analyzing the significance of such observations, Rudinger states that:

In a given molecule, some amino acids or sequences obviously owe their 'significance' to their inclusion in the pattern which is directly involved in recognition by, and binding to, the receptor. However, the fact that the existence of this pattern is dependent on a conformation stabilized by intramolecular interactions, …, implies that other amino acids or sequences contributing to this conformational stability will be no less 'significant' for the biological activity of the molecule.

(p. 5).

And, in conclusion, Rudinger states:

The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case

by painstaking experimental study. The careful design of synthetic analogues, and their evaluation in biological systems which permit separate analysis of the various phases of hormone action, is the best way to obtaining such information.

(p. 6).

Bowie, et al. (1990) Science, 247 : 1306-10 provides similar insight into the lack of reasonable predictability for the mutation of any particular protein. To wit, Bowie discuses that while many substitutions may be tolerated, in other cases substitutions may not be tolerated at all (e.g., 1306, col. 2, paragraph 2). Moreover, the significance of surface and buried amino acids while is not reasonably predictable either (pp. 1306-07), surface sites may not have any importance, but sometimes they are absolutely important due to binding (p. 1308), and predicting structure with reasonable predictability is generally limited to homologous proteins, but even that is difficult due to alignment problems (p. 1308). In general, Bowie continues to reflect the observations of Rudinger: it is not reasonably predictable that any particular amino acid change, deletion, or addition would provide a functional molecule with similar activity, and only painstaking analysis would provide such information for any particular change (e.g., pp. 1309-10).

In regards to the provisional rejection of **claim 1** under the judicial created doctrine of obviousness-type double patenting as being unpatentable over claim 4 of US non- provisional application 10/076,634 (1634 Application) applicants have stated that appropriate action will be taken if and when indication of allowable claimed subject matter requires amendment or other action in the conflicting application.

In regards to the rejection of **claims 8 and 11-12** under 35 U.S.C. 101 for claiming non-statutory subject matter, applicants have simply assert that the nucleic acid of claim 1 is a man made molecule and the host cells of **claims 8, 11 and 12** which ultimately comprise the man-made molecule demonstrate the hand of man.

Applicants' arguments have been considered but have not been found persuasive. On page 3, paragraph 005, through page 4, lines 1-2, it has been asserted that "peptides which can act as enhancer proteins are usually those which are relatively small and which are secreted naturally in large amounts over a short period, for example from glandular tissue. Peptides of this type, which include, for example, snake venom or eglin C or TAP (tick anticoagulant peptide), are distinguished by extremely good export compatibility. The invention relates to such proteins". Peptides with good transport activity are available in nature and can be expressed by HOST CELLS with no hand of man. Applicants need to amend the claims in order to distinguish the instantly claimed host cells from those available in nature as opposed to simply stating that the claimed in invention is engineered.

Conclusion

No claims are allowed

Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT B. MONDESI whose telephone number is (571)272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashed Nashaat can be reached on (571)272-0934. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Robert B Mondesi/
Primary Examiner
Art Unit 1652
February 11, 2008